

Application No. 09/719,024
Amendment dated December 23, 2003
Reply to Office action of October 21, 2003
Docket Number 22727/04080

REMARKS/ARGUMENTS

Claims 7-9, 12, 13, 17, 18, 20, 23, and 25-28 are pending in this application. Claims 7-9, 12, 13, 17, 18, 20, 23, and 25-28 are rejected. The amendments do not introduce any new matter. In consideration of the amendments and the following remarks, reconsideration of claims 7-9, 12, 13, 17, 18, 20, 23, and 25-28 is respectfully requested.

Claim Rejections - 35 USC § 112, second paragraph

Claims 7-9, 12, 13, 17, 18, 20, 23 and 25-28 under are rejected under 35 U.S.C. §112, second paragraph.

Claim 7 and its dependent claims have been amended for clarity to remove the terms "modified" and "gene," and to eliminate reference in claims 7 and 8 to specific amino acid positions. Claim 13 has been amended to eliminate reference to "the central region." It is believed that the amendments render moot the rejection of claim 7 and its dependent claims as being unclear.

As recited in amended claims 7-9, 12, 13, 25, 26 and 28, the terms "carboxy-terminal acidic activation domain" and "cysteine-histidine domain" have been used to refer to two functional domains of the protein product of the Begomovirus AL2 open reading frame. Throughout the specification there are descriptions of the features of these functional domains, including on page 2, lines 25-33, which provides description of the physical and structural properties of the highly conserved AL2 gene product, and identifies the amino acid positions and conserved structural motifs of the cysteine-histidine and carboxy terminal domains. Additional examples of references to and description of these domains are found on page 1, lines 15-23, page 7, lines 4-11, and page 16, lines 19-21.

The Patent Office has stated that the application does not provide the frame of reference for the amino acids which define each of these domains. The Patent Office has also suggested that the application does not provide information regarding the structural motifs that designate these domains. Applicant respectfully submits that the specification, figures, and the sequence listings together provide all of this information. Figure 1 shows an alignment of the amino acid sequences for several transcriptional activator proteins (AL2 gene products) from different Begomoviruses. The specification, on page 2, lines 25-33, provides a description of the orientation of the aligned sequences of Figure 1 as being from the amino (N) to carboxy (C)

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terminal. All but one of the AL2 gene products shown in Figure 1 is 129 amino acids in length (see SEQ ID NOs: 1-13 for statement of lengths). Every one of the sequences shown in the alignment of Figure 1 begins at the amino terminus with the amino acid methionine. Except for a single gap in these sequences, shown between positions 45 and 46 in the alignment (to accommodate a variation in length of one of the AL2 gene products), the sequences of the AL2 gene products are otherwise uninterrupted, and are shown in contiguous order from the amino terminus through the carboxy terminal amino acid.

The specification also provides a great deal of description of the structural motifs of these domains. Applicant has provided description of the structural motif of the cysteine-histidine domain. This domain is 20 amino acids in length (see page 1, lines 21-23), is adjacent to the N terminal region of the protein, and is characterized by a series of strictly conserved cysteine and histidine residues (see page 2, lines 28-33). The cysteine-histidine domain is involved in SNF-1 kinase binding; mutations in this region diminish or destroy SNF-1 kinase binding (see page 8, lines 19-20 and page 17, lines 12-14).

Applicant has provided description of the carboxy terminal acidic activation domain as the terminal 46 amino acids at the carboxy terminus of the protein (see page 1, lines 19-21, and page 8, lines 2-4), and has shown that the most highly conserved 15 amino acids at the carboxy terminus are sufficient to activate transcription (see page 14, lines 1-3). Applicant has reported that the carboxy terminal region of the AL2 gene product functions in activation of transcription, and that mutations in this region, particularly deletion or substitution of highly conserved acidic and hydrophobic residues, reduce or eliminate transcription activation (see page 16, lines 1-9).

Applicant respectfully submits that it has provided a frame of reference for the amino acids which define each of the carboxy terminal and cysteine-histidine domains, and that it has likewise provided description of the structural and functional features which define these regions. Accordingly, Applicant respectfully requests withdrawal of this rejection.

Claim Rejections - 35 USC § 112, first paragraph, written Description

Claims 7-9, 12, 13, 17, 18, 20, 23 and 25-28 have been rejected under §112, first paragraph.

The Patent Office has stated that no "there is no structural description of what comprises

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the modified transcription activator protein,” and the language of claim 7 “describes an infinite number of additions, deletions, or replacements of one or more amino acids, or combinations, with no size of the product defined, and without any recitation of function.”

Claim 7, as amended, recites a mutant Begomoviral transcription activator protein in which there is a first mutation in the open reading frame encoding the carboxy terminal domain of the protein, and a second mutation in the open reading frame encoding the cysteine-histidine domain of the protein, wherein the encoded mutant protein lacks or has diminished transcription activation and SNF-1 binding activities as compared to a wild-type protein.

Applicant submits that claim 7, as amended, does identify both structural and functional features of the mutant transcriptional activation protein, and is supported in the specification by description of a variety of specific mutant forms of the protein. The recited mutant proteins all have mutations in both the carboxy terminal acidic activation domain and the cysteine-histidine domain. Extensive information has been provided in the specification regarding the structures of these two domains, and the particular amino acids that define each domain in this highly conserved protein. These mutant proteins are characterized by alterations in their SNF-1 kinase binding and transcription activation functions. Applicant has provided many examples of mutations that have been introduced in the AL2 open reading frame to provide mutant transcriptional activation protein, including. For example, Applicant has provided an examples of mutant proteins in which deletions in the carboxy terminal domain, particularly deletions of one or more of the 15 terminal amino acids, result in loss of transcription activation activity (see page 13, lines 24-32). Applicant has also shown that substitution of acidic amino acids in the 15 terminal amino acids in the carboxy terminal domain result in reduction or nearly complete loss of transcription activation (see page 16, lines 1-9). Applicant has also provided an example of mutations to the cysteine-histidine domain wherein replacement of a positively charged histidine residue with a neutral alanine residue resulted in loss of SNF-1 kinase binding activity.

With all of this detail regarding the structure and functional properties of a variety of forms of mutant Begomovirus transcription activator protein, one of ordinary skill in the relevant art would surely recognize that Applicant had possession of the claimed invention at the time the application was filed. For all of the foregoing reasons, Applicant submits that claim 7 and all of its dependent claims are fully supported by the written description. Applicant respectfully

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requests withdrawal of the rejection of these claims.

Claim Rejections - 35 USC § 112, first paragraph, scope of enablement

Claims 7-9, 12, 13, 17, 18, 20, 23 and 25-28 have been rejected under §112, first paragraph, as not enabled.

Applicant respectfully submits that there is more than ample guidance provided in the specification to enable one of ordinary skill in the art to prepare the mutant transcriptional activator protein as recited in claim 7 and its dependent claims, as amended. Applicant has described the structural features of the AL2 open reading frame and the AL2 gene product, and has provided a multitude of examples of different wild-type forms of AL2 (see Figure 1, Table 1, and SEQ ID NOs 1-13 and 76-147). Applicant has identified regions of the protein, namely the carboxy terminal and cysteine-histidine domains, where mutations can be introduced to provide mutant protein having the functional properties as recited in amended claim 7. Applicant has also taught a number of examples of mutations using primer construct sequences. (See example 21 and Figure 2.

The Patent Office has indicated that claim 7 and its dependent claims provide for an "infinite number" of possible mutations, and that "neither the size of the gene nor that of the corresponding protein is able to be defined." Applicant submits that the law does not require Applicant to identify every discrete species within a genus, and it does not impose a limit on the possible size of a genus. Reading Applicant's disclosure, one of ordinary skill could identify and select an AL2 open reading frame from a Begomovirus of interest, and use known techniques to prepare mutations in the portions of the open reading frame that encode the carboxy terminal and cysteine-histidine domains. Such mutations may be selected from those shown in the examples, or other mutations contemplated by Applicant, as described in the specification. Using techniques described by Applicant or otherwise known in the art, one of ordinary skill could readily test the resulting mutant protein products to confirm the effect of the mutations on functional activity of the protein. There may be a large number of possible mutants in the genes contemplated by claim 7, as amended, requiring considerable effort on the part of one of ordinary skill in the art to prepare and test such species. However, as stated by the Board of

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Patent Appeals and interference, "a considerable amount of experimentation is permissible, if it is merely routine, or if the specification in question provides a reasonable amount of guidance with respect to the direction in which the experimentation should proceed to enable the determination of how to practice the a desired embodiment for the invention claimed." (Ex parte Forman, 230 USPQ 546, 547 (Bd. Pat. App. & Int., 1986) Applicant has provided reasonable guidance in the making of mutant transcriptional activation protein, and has identified the direction in which efforts to produce additional mutants should proceed -- namely by making mutations in the carboxy and cysteine-histidine domains which result in alteration of SNF-1 kinase binding and transcription activation function. Accordingly, Applicant submits that claim 7 and its dependent claims are enabled, and respectfully requests withdrawal of the rejection.

In view of the above-described amendments and remarks, it is submitted that claims 7-9, 12, 13, 17, 18, 20, 23 and 25-28 are in condition for allowance. Prompt notice of such allowance is respectfully requested.

Respectfully submitted,

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